

AMENDMENTS TO THE CLAIMS

1-179. (Canceled)

180. (Currently Amended) An infectious chimeric parainfluenza virus (PIV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete open reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequences operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said partial or complete PIV genome or antigenome comprising a polynucleotide encoding a wild-type L protein of the PIV;

said infectious chimeric PIV being attenuated for replication at least 10-fold ~~being attenuated for replication at least 10-fold~~ in the respiratory tract of a primate host infected with said chimeric PIV compared to the corresponding wild-type PIV.

181. (Previously Presented) An infectious chimeric parainfluenza virus (PIV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequence operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said heterologous gene(s) or genome segment(s) being inserted into the PIV genome or antigenome at one or more site(s) selected from the group consisting of a site between the P and M open reading frames, a site between the N and P open reading frames, a site between the HN and L open reading frames and a site between the 3' leader and the N open reading frame.

182. (Previously Presented) The infectious chimeric PIV of claim 181, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Val96 of the N protein, Ser389 of the N protein, Ile96 of the C protein, Ile420 of the F protein, Ala450 of the F protein, Val384 of the HN protein, Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein, nucleotide 23 of the 3' leader sequence, nucleotide 24 of the 3' leader sequence, nucleotide 28 of the 3' leader sequence, nucleotide 45 of the 3' leader sequence and nucleotide 62 in the N gene start sequence.

183. (Previously Presented) The infectious chimeric PIV of claim 181, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Tyr942 of the L protein, Leu992 of the L protein and Thr1558 of the L protein.

184. (Previously Presented) The infectious chimeric PIV of claim 180, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

185. (Previously Presented) The infectious chimeric PIV of claim 181, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

186. (Previously Presented) The infectious chimeric PIV of claim 182, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

187. (Previously Presented) The infectious chimeric PIV of claim 183, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

188. (Previously Presented) The infectious chimeric PIV of claim 181, in which the partial or complete PIV genome or antigenome further includes mutations at a position corresponding to a position in the genome of HPIV3 of Tyr942 of the L protein, Leu992 of the L protein and Thr1558 of the L protein.

189. (Previously Presented) The infectious chimeric PIV of claim 188, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

190. (Previously Presented) An infectious chimeric parainfluenza virus (PIV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete open reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequences operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said partial or complete PIV genome or antigenome including a mutation encoding a substitution of the amino acid corresponding to amino acid 456 of the L protein of HPIV3 by another amino acid.

191. (Previously Presented) The infectious chimeric PIV of claim 190, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Val96 of the N protein, Ser389 of the N protein, Ile96 of the C protein, Ile420 of the F protein, Ala450 of the F protein, Val384 of the HN protein, Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein, nucleotide 23 of the 3' leader sequence, nucleotide 24 of the 3' leader sequence, nucleotide 28 of the 3' leader sequence, nucleotide 45 of the 3' leader sequence and nucleotide 62 in the N gene start sequence.

192. (Previously Presented) The infectious chimeric PIV of claim 190, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein.

193. (Previously Presented) The infectious chimeric PIV of claim 190, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

194. (Previously Presented) The infectious chimeric PIV of claim 191, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

195. (Previously Presented) The infectious chimeric PIV of claim 192, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

196. (Currently Amended) An infectious chimeric parainfluenza virus (PIV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV genome or antigenome of said PIV, comprising a plurality of heterologous genome segments encoding a plurality of antigenic determinants of one or more proteins of one or more heterologous pathogens to form a chimeric PIV genome or antigenome;

wherein said heterologous genome segments are operatively linked to a gene start sequence and to a gene end sequence of said PIV,

and wherein chimeric PIV is attenuated at least 10-fold in the respiratory tract of a primate host compared to the corresponding wild-type PIV.

197. (Previously Presented) The infectious chimeric PIV of claim 196, wherein the partial or complete genome or antigenome encodes a wild-type L protein of said PIV.

198. (Previously Presented) The infectious chimeric PIV of claim 196, in which at least one of the plurality of antigenic determinants are from a glycoprotein of said heterologous pathogen.

199. (Previously Presented) The infectious chimeric PIV of claim 197, in which at least one of the plurality of antigenic determinants are from a glycoprotein of said heterologous pathogen.

200. (Previously Presented) The infectious chimeric PIV of any one of claims 180-199 that is a sub-viral particle.

201. (Previously Presented) An immunogenic composition comprising the infectious chimeric PIV of any one of claims 180-199.

202. (Previously Presented) An immunogenic composition comprising the infectious chimeric PIV of claim 200.

203. (Currently Amended) An isolated polynucleotide encoding a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete open reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequences operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said partial or complete PIV genome or antigenome comprising a polynucleotide encoding a wild-type L protein of the PIV;

said partial or complete chimeric PIV genome or antigenome providing an infectious chimeric PIV being attenuated for replication at least 10-fold in the respiratory tract of a primate host infected with said chimeric PIV compared to the corresponding wild-type PIV.

204. (Previously Presented) An isolate polynucleotide encoding a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequence operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said heterologous gene(s) or genome segment(s) being inserted into the PIV genome or antigenome at one or more site(s) selected from the group consisting of a site between the P and M open reading frames, a site between the N and P open reading frames, a site between the HN and L open reading frames and a site between the 3' leader and the N open reading frame.

205. (Previously Presented) The isolated polynucleotide of claim 203, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Val96 of the N protein, Ser389 of the N protein, Ile96 of the C protein, Ile420 of the F protein, Ala450 of the F protein, Val384 of the HN protein, nucleotide 23 of the 3' leader sequence, nucleotide 24 of the 3' leader sequence, nucleotide 28 of the 3' leader sequence, nucleotide 45 of the 3' leader sequence and nucleotide 62 in the N gene start sequence.

206. (Previously Presented) The isolated polynucleotide of claim 204, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Val96 of the N protein, Ser389 of the N protein, Ile96 of the C protein, Ile420 of the F protein, Ala450 of the F protein, Val384 of the HN protein, Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein, nucleotide 23 of the 3' leader sequence, nucleotide 24 of the 3' leader sequence, nucleotide 28 of the 3' leader sequence, nucleotide 45 of the 3' leader sequence and nucleotide 62 in the N gene start sequence.

207. (Previously Presented) The isolated polynucleotide of claim 204, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Tyr942 of the L protein, Leu992 of the L protein and Thr1558 of the L protein.

208. (Previously Presented) The isolated polynucleotide of claim 203, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

209. (Previously Presented) The isolated polynucleotide of claim 207, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

210. (Previously Presented) The isolated polynucleotide of claim 205, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

211. (Previously Presented) The isolated polynucleotide of claim 206, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

212. (Previously Presented) The isolated polynucleotide of claim 207, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

213. (Previously Presented) An isolated polynucleotide that encodes a partial or complete PIV genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding a complete open reading frame or one or more antigenic determinant(s) of one or more heterologous pathogen(s) operably linked to regulatory sequences operable in said PIV genome or antigenome to form a chimeric PIV genome or antigenome;

said partial or complete PIV genome or antigenome including a mutation encoding a substitution of the amino acid corresponding to amino acid 456 of the L protein of HPIV3 by another amino acid.

214. (Previously Presented) The isolated polynucleotide of claim 213, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Val96 of the N protein, Ser389 of the N protein, Ile96 of the C protein, Ile420 of the F protein, Ala450 of the F protein, Val384 of the HN protein, Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein, nucleotide 23 of the 3' leader sequence, nucleotide 24 of the 3' leader sequence, nucleotide 28 of the 3' leader sequence, nucleotide 45 of the 3' leader sequence and nucleotide 62 in the N gene start sequence.

215. (Previously Presented) The isolated polynucleotide of claim 213, in which the partial or complete PIV genome or antigenome further includes at least one mutation at a position corresponding to a position in the genome of HPIV3 selected from the group consisting of Tyr942 of the L protein, Leu992 of the L protein, Thr1558 of the L protein.

216. (Previously Presented) The isolated polynucleotide of claim 213, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

217. (Previously Presented) The isolated polynucleotide of claim 214, in which the partial or complete PIV genome or antigenome comprises at least one glycoprotein open reading frame or segment thereof of another PIV.

218. (Currently Amended) An isolated polynucleotide encoding a partial or complete PIV genome or antigenome of said PIV, comprising a plurality of heterologous genome segments encoding a plurality of antigenic determinants of one or more heterologous pathogens to form a chimeric PIV genome or antigenome;

wherein said heterologous genome segments are operatively linked to a gene start sequence and to a gene end sequence of said PIV,

and wherein chimeric PIV is attenuated at least 10-fold in the respiratory tract of a primate host compared to the corresponding wild-type PIV.

219. (Previously Presented) The isolated polynucleotide of claim 218, that comprises a wild-type L gene of said PIV.

220. (Previously Presented) The isolated polynucleotide of claim 218, in which at least one of the plurality of antigenic determinants are from a glycoprotein of said heterologous pathogen.

221. (Previously Presented) The isolated polynucleotide of claim 219, in which at least one of the plurality of antigenic determinants are from a glycoprotein of said heterologous pathogen.

222. (Previously Presented) A vector comprising, in operative linkage,
i) a promoter operative in a mammalian cell or operable *in vitro*;
ii) a polynucleotide of any one of claims 203-221;
iii) a transcription terminator sequence operable in a mammalian cell or *in vitro*.